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Promoter Methylation Status and Expression Levels of RASSF1A Gene in Different Phases of Acute Lymphoblastic Leukemia (ALL)

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ABSTRACT

Background: Although the precise pathogenesis of acute lymphoblastic leukemia (ALL) remains unclear, studying gene-regulating mechanisms during ALL pathogeneses may shed light on the underlying mechanisms driving malignant behavior. There is some evidence showing the promoter hypermethylation and silencing of RASSF1A tumor suppressor gene in ALL cells; however, there is a lack of evidence for whether the gene indeed alters during different phases of ALL or in response to therapy. Thus, the current study aimed to clarify this issue using groups of adult ALL patients who have been scarcely investigated regarding expression levels and promoter methylation status.

Materials and Methods: In this case/control study, the expression levels and methylation status of the gene promoter was evaluated using quantitative real-time PCR and methylation-specific PCR (MSP), respectively in adults with ALL. The study included peripheral blood of patients with newly diagnosed ALL (n=10), complete remission (CR) (n=10), or relapse (n=10), and 10 control samples from healthy individuals.

Results: MSP results revealed an unmethylated status for almost all patients and control samples, except a case with relapsing ALL, which showed a hemimethylated pattern. RASSF1A also showed no difference in terms of gene expression in the patients compared with the control group ($p>0.05$).

Conclusion: The results revealed an up-regulation of RASSF1A tumor suppressor in adult ALL patients experiencing CR, suggesting this to be a marker of therapy response. However, further investigations using more sensitive methylation detecting tools with larger sample sizes may better clarify the involvement of the promoter methylation of RASSF1A in these patients.

Keywords: Expression level; Methylation pattern; Ras association domain family member 1(RASSF1A) gene; Acute lymphoblastic leukemia (ALL)

INTRODUCTION

Acute lymphoblastic leukemia (ALL) is characterized by the excessive accumulation of lymphoblasts and lymphoid progenitors. Although ALL is the most common type of leukemia in children (25%), there is also a peak of incidence in adults[1]. The disease had been regarded incurable until 1970, which caused fatal consequences in the affected individuals[2]. A novel therapeutic development could overcome the irreversible